

REMARKS

I. Amendments

Claims 1-23 have been canceled, including claims 1-7, 9, 11-16 and 23, which were withdrawn from consideration as being drawn to non-elected inventions. Claims 30-33 have been added. Claim 28 has been amended. The amended and newly added claims do not add or constitute new matter, and are completely supported by the application as originally filed. Support may be found throughout the specification and in the originally filed claims. Specifically, support for the transgenic mice recited in claims 24-27, 29-31 and 33 may be found, for example, in original claims 18-22 and at page 53, line 13 through page 54, line 10, of the specification. Support for the method of producing the transgenic mouse recited in claims 28 and 32 may be found, for example, at page 11, line 19 through page 18, line 4, and at page 53 lines 16-29, of the specification.

The amendments to the claims are made without prejudice to the pending or now-canceled claims or to any subject matter pursued in related applications. Moreover, the amendments are made solely to place the claims of the application in condition for allowance in response to the final rejection, and are not intended to limit the scope of the invention. The Applicant reserves the right to prosecute any canceled subject matter at a later time or in a later filed divisional, continuation or continuation-in-part application.

Upon entry of the foregoing amendments, claims 24-33 are pending in the instant application.

II. Rejections

A. Rejections under 35 U.S.C. § 112, second paragraph

Claims 28-29 were rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. The Applicant respectfully traverses this rejection.

Specifically, with respect to the term “murine” in claim 28, the Examiner has stated that “the term murine encompasses both mice and rats.” The Examiner states that use of the term in step (b), which recites introducing a CRFR2 gene targeting construct into a **murine** embryonic stem cell, renders the claim indefinite because it is unclear how a transgenic mouse can be produced when using a rat embryonic stem cell. The Examiner has suggested “amending the claim to read on a mouse embryonic stem cell.” Applicant has adopted the Examiners’ suggested modification, and amended claim 28 accordingly. Claim 28 no longer recites the term

“murine” rendering this rejection moot. Therefore Applicant respectfully requests withdrawal of the rejection under 35 U.S.C. § 112, second paragraph.

Applicant submits that claims 24-33, including amended claim 28, are definite and particularly point out and distinctly claim that which Applicant regards as the invention in accordance with 35 U.S.C. § 112, second paragraph.

B. Rejections under 35 U.S.C. § 102

1. Coste et al.

Claims 24-29 were rejected under 35 U.S.C. § 102 as being anticipated by Coste *et al.*, 2000, *Nature Genetics*, 24:403-409 (“Coste”). The Applicant respectfully traverses this rejection.

Claims 24-29 are drawn to a transgenic mouse whose genome comprises a disruption in the endogenous CRFR2 gene, wherein the transgenic mouse exhibits phenotypes including decreased activity and decreased susceptibility to seizure, and a method of producing the transgenic mouse.

The Examiner asserts that Coste discloses a transgenic mouse comprising a disruption in the CRHR2 gene (interpreted to be the CRFR2 gene of the present invention), wherein the disruption results in no production of CRHR2, and wherein the mouse is created by introducing a targeting vector into ES cells, transferring the ES cells to a blastocyst and then implanting the blastocyst into a pseudopregnant female mouse, wherein said female mouse gives birth to a chimeric mouse, and breeding said chimeric mouse to produce the transgenic mouse. The Examiner asserts that, although the mouse of Coste exhibits phenotypes which differ from the claimed mouse, “any phenotypes associated with disruption of the CRFR2 gene are inherent properties of the mouse, since it does not appear that the mice are structurally different.” The Examiner has stated that the prima facie case of anticipation “can be rebutted by evidence showing that the prior art products do not necessarily possess the characteristics of the claimed product.” See MPEP § 2112.01, citing *In re Best*, 562 F.2d at 1255, 195 USPQ at 433.

A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference. See MPEP § 2131. Applicant submits that the mouse of Coste does not meet all of the limitations recited in the pending claims. More particularly, Applicant submits that the mouse of Coste does not merely exhibit phenotypes which differ from the claimed mouse, as the Examiner asserts, but exhibits

phenotypes opposite of or inconsistent with those of the claimed mouse, making it improper to assert that the phenotypes are inherent properties of the mouse. As such, the phenotypes of the claimed mouse, namely decreased activity and decreased susceptibility to seizure, not found in Coste, are sufficient to overcome the anticipation rejection.

First, the phenotypes observed by Applicant are distinct from and do not overlap the phenotypes observed by Coste. Coste states that the CRHR2 knockout mouse exhibits phenotypes including modification of the stress response (a more robust stress hormone response and elevated corticosterone levels after stress), subtle changes in anxiety-like behavior (reduced time in the center of the open-field), reduced grooming behavior, altered urocortin (Ucn) induced feeding suppression, and elevated mean arterial blood pressure and diastolic pressure (see Abstract and pages 403-406). The instant specification and pending claims do not disclose or recite any of the phenotypes observed by Coste. The claimed mouse exhibits phenotypes which include decreased activity and decreased susceptibility to seizure, which are clearly distinct from and do not overlap with the phenotypes disclosed in Coste. Furthermore, one of these phenotypes – decreased activity - is clearly inconsistent with those observed in Coste. Coste found and disclosed no difference between their CRHR2 knockout mice and wild type mice in activity level, as evidenced by no difference in total ambulation in a novel open-field between the wild-type and knockout mice (see page 404, column 1). In contrast, the claimed mouse, which exhibits decreased activity relative to wild-type mice when observed in an open-field environment, possesses a phenotype that is expressly **not possessed** by the mouse disclosed in Coste. In fact, the phenotypic observations of the Applicant, as recited in the pending claims, are inconsistent with or counter to the phenotypic observations of Coste, demonstrating that the limitations recited in the pending claims are not merely inherent properties of the mouse of Coste, but that the claimed mouse exhibits opposite or contradictory properties.

Furthermore, it has not been established that the claimed mouse and the mouse of Coste are “identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes” as asserted by the Examiner. Specifically, the Examiner has interpreted the gene disrupted in Coste to be the same gene disrupted in the claimed mouse and has stated that “it does not appear that the mice are structurally different.” However, it has not been established that the mouse of Coste comprises the same disruption or that the disruption is in an identical gene as the gene disrupted in the claimed mouse. This is evidenced by the

phenotypes of the claimed mouse, which differ from, and are in fact inconsistent with, those of the mouse of Coste as noted above, and also by the lack of disclosure in Coste regarding the nucleotide sequence of the disrupted CRHR2 gene.

For these reasons, Applicants believe that the claimed mouse and the mouse of Coste are not structurally identical, and thus the phenotypic limitations recited in the pending claims should be sufficient to overcome the anticipation rejection. However, as the Office Action has been made final, Applicant is making a genuine attempt to place the pending claims in condition for allowance. Therefore, Applicant has added claims 30-33, which merely narrow the scope of the pending claims rejected by the Examiner as anticipated by Coste in order to overcome the rejection. New claims 30-33 recite a transgenic mouse and method of producing the transgenic mouse comprising a disruption in the CRFR2 gene, wherein the disruption deletes nucleotides 441 through 582 of the CRFR2 gene, resulting in a phenotype of decreased activity or decreased susceptibility to seizure. Coste fails to teach or even suggest this location and extent of disruption of the CRFR2 gene, and further fails to disclose or suggest a phenotype of decreased activity or decreased susceptibility as a result of such a disruption, as recited in these claims. Applicant submits that the issue of the inherency of the phenotypes exhibited by the claimed mouse no longer applies to these claims, as Coste fails to teach or disclose every claimed element.

In light of the disclosure in Coste regarding activity levels discussed above, Applicant submits that claims 24-29 are not anticipated by Coste. However, Applicant has submitted new claims 30-33, which clearly are not anticipated by Coste. Applicant respectfully requests reconsideration and withdrawal of the rejection of claims 24-29, and allowance of claims 24-33.

2. Bale *et al.*

Claims 24-29 were also rejected under 35 U.S.C. § 102 as being anticipated by Bale *et al.*, 2000, *Nature Genetics*, 24:410-414 (“Bale”). The Applicant respectfully traverses this rejection.

Claims 24-29 are drawn to a transgenic mouse whose genome comprises a disruption in the endogenous CRFR2 gene, wherein the transgenic mouse exhibits phenotypes including decreased activity and decreased susceptibility to seizure, and a method of producing the transgenic mouse.

The Examiner asserts that Bale discloses a transgenic mouse comprising a disruption in the CRHR2 gene (interpreted to be the CRFR2 gene of the present invention), wherein the disruption results in no production of CRHR2, and wherein the mouse is created by introducing a targeting vector into ES cells, transferring the ES cells to a blastocyst and then implanting the blastocyst into a pseudopregnant female mouse, wherein said female mouse gives birth to a chimeric mouse, and breeding said chimeric mouse to produce the transgenic mouse. The Examiner asserts that, although the mouse of Bale exhibits phenotypes which differ from the claimed mouse, “any phenotypes associated with disruption of the CRFR2 gene are inherent properties of the mouse, since it does not appear that the mice are structurally different.” The Examiner has stated that the prima facie case of anticipation “can be rebutted by evidence showing that the prior art products do not necessarily possess the characteristics of the claimed product.” See MPEP § 2112.01, citing *In re Best*, 562 F.2d at 1255, 195 USPQ at 433.

A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference. See MPEP § 2131. Applicant submits that the mouse of Bale does not meet all of the limitations recited in the pending claims. More particularly, Applicant submits that the mouse of Bale does not merely exhibit phenotypes which differ from the claimed mouse, as the Examiner asserts, but exhibits **phenotypes opposite of or inconsistent with** those of the claimed mouse, making it improper to assert that the phenotypes are inherent properties of the mouse.

First, the phenotypes observed by Applicant are distinct from and do not overlap the phenotypes observed by Bale. Bale discloses phenotypes of the CRHR2 knockout mouse including hypersensitivity of the hypothalamic-pituitary-adrenal (HPA) axis to stress, increased anxiety-like behavior (reduced time and number of entries into the open arms of the elevated plus maze), and decreased food intake following food deprivation (see Abstract and pages 411-412). The instant specification and pending claims do not disclose or recite any of the phenotypes observed by Bale. The claimed mouse exhibits phenotypes which include decreased activity and decreased susceptibility to seizure, which are clearly distinct from the phenotypes disclosed in Bale. Furthermore, as was noted in Coste, one of these phenotypes – decreased activity – is inconsistent with those observed in Bale. Like Coste, Bale found and disclosed no difference between their CRHR2 knockout mice and wild type mice in activity level – “the increase in anxiety-like behaviour was not due to altered locomotor activity, as overall activity in

the closed arm entries and total arm entries was not different between the two groups” (knockout and wild-type in the elevated-plus maze, see page 411, column 2 and Fig. 4c/d). In contrast, the claimed mouse, which exhibits decreased activity relative to wild-type mice when observed in an open-field environment, possesses a phenotype that is expressly **not possessed** by the mouse described in Bale. In fact, the phenotypic observations of the Applicant, as recited in the pending claims, are inconsistent with or counter to the phenotypic observations of Bale, demonstrating that the limitations recited in the pending claims are not merely inherent properties of the Bale mouse, but that the Bale mouse and the claimed mouse exhibit opposite or contradictory properties.

Furthermore, it has not been established that the claimed mouse and the mouse of Bale are “identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes” as asserted by the Examiner. Specifically, the Examiner has interpreted the gene disrupted in Bale to be the same gene disrupted in the claimed mouse and has stated that “it does not appear that the mice are structurally different.” However, it has not been established that the mouse of Bale comprises the same disruption or that the disruption is in an identical gene as the gene disrupted in the claimed mouse. This is evidenced by the phenotypes of the claimed mouse, which are clearly inconsistent with those of the mouse of Bale as noted above, and also by the lack of disclosure in Bale regarding the nucleotide sequence of the disrupted CRHR2 gene.

For the reasons set forth above, Applicants believe that the claimed mouse and the mouse of Bale are not structurally identical, and thus the phenotypic limitations recited in the pending claims should be sufficient to overcome the anticipation rejection. However, as noted previously, Applicant is making a genuine attempt to place the pending claims in condition for allowance. Therefore, Applicant has added claims 30-33, which merely narrow the scope of the pending claims rejected by the Examiner as anticipated by Bale in order to overcome the rejection. New claims 30-33 recite a transgenic mouse and method of producing the transgenic mouse comprising a disruption in the CRFR2 gene, wherein the disruption deletes nucleotides 441 through 582 of the CRFR2 gene, resulting in a phenotype of decreased activity or decreased susceptibility to seizure. Bale fails to teach or even suggest this location and extent of disruption of the CRFR2 gene, and further fails to disclose or suggest a phenotype of decreased activity or decreased susceptibility as a result of such a disruption, as recited in these claims. Applicant

submits that the issue of the inherency of the phenotypes exhibited by the claimed mouse no longer applies to these claims, as Bale fails to teach or disclose every claimed element.

In view of the distinct phenotypes observed by Bale and Applicant regarding activity levels, Applicant submits that claims 24-29 are not anticipated by Bale. However, Applicant has submitted new claims 30-33, which clearly are not anticipated by Bale. Applicant respectfully requests reconsideration and withdrawal of the rejection of claims 24-29 and allowance of claims 24-33.

3. Kishimoto *et al.*

The Examiner has also rejected claims 24-29 under 35 U.S.C. § 102 as being anticipated by Kishimoto *et al.*, 2000, *Nature Genetics*, 24:415-419 (“Kishimoto”). The Applicant respectfully traverses this rejection.

Claims 24-29 are drawn to a transgenic mouse whose genome comprises a disruption in the endogenous CRFR2 gene, wherein the transgenic mouse exhibits phenotypes including decreased activity and decreased susceptibility to seizure, and a method of producing the transgenic mouse.

The Examiner asserts that Kishimoto discloses a transgenic mouse comprising a disruption in the CRHR2 gene (interpreted to be the CRFR2 gene of the present invention), wherein the disruption results in no production of CRHR2, and wherein the mouse is created by introducing a targeting vector into ES cells, transferring the ES cells to a blastocyst and then implanting the blastocyst into a pseudopregnant female mouse, wherein said female mouse gives birth to a chimeric mouse, and breeding said chimeric mouse to produce the transgenic mouse. The Examiner asserts that, although the mouse of Kishimoto exhibits phenotypes which differ from the claimed mouse, “any phenotypes associated with disruption of the CRFR2 gene are inherent properties of the mouse, since it does not appear that the mice are structurally different.” The Examiner has stated that the *prima facie* case of anticipation “can be rebutted by evidence showing that the prior art products do not necessarily possess the characteristics of the claimed product.” See MPEP § 2112.01, citing *In re Best*, 562 F.2d at 1255, 195 USPQ at 433.

A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference. See MPEP § 2131. Applicant submits that every element as recited in the pending claims is not found in Kishimoto. More particularly, Applicant submits that the CRHR2 deficient mouse of Kishimoto exhibits

phenotypes which differ from the claimed mouse, and, in fact, exhibits **phenotypes opposite of or inconsistent with** those of the claimed mouse, making it improper to assert that the phenotypes of the claimed mouse are inherent properties of the mouse described in Kishimoto.

First, the phenotypes observed by Applicant are distinct from and do not overlap the phenotypes observed by Kishimoto. Kishimoto observed a phenotype of increased anxiety-like behavior, as shown in elevated plus-maze, dark-light emergence and open-field tests (see Abstract and pages 415, column 1 through 416). The instant specification and pending claims do not disclose or recite a phenotype of increased anxiety in the CRFR2 deficient mice, as Kishimoto demonstrated. Rather, the claimed mouse exhibits phenotypes which include decreased activity and decreased susceptibility to seizure, which are distinct from the increased anxiety phenotype disclosed in Kishimoto. Furthermore, one of the phenotypes of the claimed mouse – decreased activity – is clearly inconsistent with the observations of Kishimoto. Like Coste and Bale, Kishimoto reported no difference between their CRHR2 knockout mice and wild type mice in locomotor activity – “locomotor activity of male *Crhr2* $-/-$ and *Crhr2* $+/-$ mice was not affected” (see page 415, column 2 and Fig. 2a). In contrast, the claimed mouse, which exhibits decreased activity relative to wild-type mice when observed in an open-field environment, possesses a phenotype that is expressly **not possessed** by the mouse described in Kishimoto. In fact, the phenotypic observations of the Applicant, as recited in the pending claims, are counter to the phenotype observed in Kishimoto, demonstrating that the limitations recited in the pending claims are not merely inherent properties of the mouse of Kishimoto, but that the mouse of Kishimoto and the claimed mouse exhibit opposite or contradictory properties, making them distinct each from the other.

Furthermore, it has not been established that the claimed mouse and the mouse of Kishimoto are “identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes” as asserted by the Examiner. Specifically, the Examiner has interpreted the gene disrupted in Kishimoto to be the same gene disrupted in the claimed mouse and has stated that “it does not appear that the mice are structurally different.” However, it has not been established that the mouse of Kishimoto comprises the same disruption or that the disruption is in an identical gene as the gene disrupted in the claimed mouse. This is evidenced by the phenotype of the claimed mouse, which is clearly inconsistent with those of the

mouse of Kishimoto as noted above, and also by the lack of disclosure in Kishimoto regarding the nucleotide sequence of the disrupted CRHR2 gene.

For these reasons, Applicants believe that the claimed mouse and the mouse of Kishimoto are not identical, and thus the phenotypic limitations recited in the pending claims should be sufficient to overcome the anticipation rejection. However, as noted previously, Applicant is making a genuine attempt to place the pending claims in condition for allowance. Therefore, Applicant has added claims 30-33, which merely narrow the scope of the pending claims rejected by the Examiner as anticipated by Kishimoto in order to overcome the rejection. New claims 30-33 recite a transgenic mouse and method of producing the transgenic mouse comprising a disruption in the CRFR2 gene, wherein the disruption deletes nucleotides 441 through 582 of the CRFR2 gene, resulting in a phenotype of decreased activity or decreased susceptibility to seizure. Kishimoto fails to teach or suggest the specific location and extent of disruption of the CRFR2 gene, and further fails to disclose or suggest a phenotype of decreased activity or decreased susceptibility as a result of such a disruption, as recited in these claims. Applicant submits that the issue of the inherency of the phenotypes exhibited by the claimed mouse no longer applies to these claims, as Kishimoto clearly fails to teach or disclose every claimed element.

In view of the disclosure regarding activity level discussed above, Applicant submits that claims 24-29 are not anticipated by Kishimoto. However, Applicant has submitted new claims 30-33, which clearly are not anticipated by Kishimoto. Applicant respectfully requests reconsideration and withdrawal of the rejection of claims 24-29 and allowance of claims 24-33.

4. Lee *et al.*

Finally, the Examiner has rejected claims 24-29 under 35 U.S.C. § 102 as being anticipated by Lee *et al.*, U.S. Serial No. 6,353,152, effective filing date July 15, 1999 (“Lee”). The Applicant respectfully traverses this rejection.

Claims 24-29 are drawn to a transgenic mouse whose genome comprises a disruption in the endogenous CRFR2 gene, wherein the transgenic mouse exhibits phenotypes including decreased activity and decreased susceptibility to seizure, and a method of producing the transgenic mouse.

According to the Examiner, Lee discloses a transgenic mouse comprising a disruption in the CRHR2 gene (interpreted to be the CRFR2 gene of the present invention), wherein the

disruption results in no production of CRHR2, and wherein the mouse is created by introducing a targeting vector into ES cells, transferring the ES cells to a blastocyst and then implanting the blastocyst into a pseudopregnant female mouse, wherein said female mouse gives birth to a chimeric mouse, and breeding said chimeric mouse to produce the transgenic mouse. The Examiner asserts that, although the mouse of Lee exhibits phenotypes which differ from the claimed mouse, “any phenotypes associated with disruption of the CRFR2 gene are inherent properties of the mouse, since it does not appear that the mice are structurally different.” The Examiner has stated that the prima facie case of anticipation “can be rebutted by evidence showing that the prior art products do not necessarily possess the characteristics of the claimed product.” See MPEP § 2112.01, citing *In re Best*, 562 F.2d at 1255, 195 USPQ at 433.

A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference. See MPEP § 2131. Applicant submits that the mouse of Lee does not meet all of the limitations recited in the pending claims. More particularly, Applicant submits that the CRHR2 deficient mouse of Lee does not merely exhibit different phenotypes from those of the claimed mouse, as the Examiner asserts, but exhibits **phenotypes opposite of or inconsistent with** those of the claimed mouse, making it improper to assert that the phenotypes are inherent properties of the mouse.

First, the phenotypes observed by Applicant are distinct from and do not overlap the phenotypes observed by Lee. Lee observed phenotypes similar to those of the other prior art references, including increased anxiety-like behavior, decreased food intake after food deprivation, and hypersensitivity to stress (see Abstract and Example 5 through Example 9). The instant specification and pending claims do not disclose or recite any of the phenotypes for the CRFR2 deficient mice demonstrated by Lee. Rather, the claimed mouse exhibits phenotypes which include decreased activity and decreased susceptibility to seizure, which are distinct from the phenotypes disclosed in Lee. Furthermore, one of these phenotypes – decreased activity – is clearly inconsistent with those observed by Lee. Like the other prior art references, Lee reported no difference between the locomotor activity of the CRHR2 knockout mice and wild type mice (see Example 7 for elevated plus maze and Example 9 for open-field). In contrast, the claimed mouse, which exhibits decreased activity relative to wild-type mice when observed in an open-field environment, possesses a phenotype that is expressly **not possessed** by the mouse described in Lee. In fact, the decreased activity seen in the claimed mouse (as recited in the pending

claims) is inconsistent with the observations of Lee (normal activity levels), demonstrating that the limitations recited in the pending claims are not merely inherent properties of the mouse of Lee, but that the mouse of Lee and the claimed mouse exhibit properties which contradict each other.

Furthermore, it has not been established that the claimed mouse and the mouse of Lee are “identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes” as asserted by the Examiner. Specifically, the Examiner has interpreted the gene disrupted by Lee to be the same gene disrupted in the claimed mouse and has stated that “it does not appear that the mice are structurally different.” However, it has not been established that the mouse of Lee comprises an identical disruption or that the disruption is in an identical gene as in the claimed mouse. This is evidenced by the phenotype of the claimed mouse, which is clearly inconsistent with those of the Lee mouse as noted above, and also by the lack of disclosure in Lee regarding the nucleotide sequence of the disrupted CRHR2 gene.

For these reasons, Applicants believe that the claimed mouse and the mouse of Lee are not structurally identical, and thus the phenotypic limitations recited in the pending claims should be sufficient to overcome the anticipation rejection. However, as noted previously, Applicant is making a genuine attempt to place the pending claims in condition for allowance. Therefore, Applicant has added claims 30-33, which merely narrow the scope of the pending claims rejected by the Examiner as anticipated by Lee in order to overcome the rejection. New claims 30-33 recite a transgenic mouse and method of producing the transgenic mouse comprising a disruption in the CRFR2 gene, wherein the disruption deletes nucleotides 441 through 582 of the CRFR2 gene, resulting in a phenotype of decreased activity or decreased susceptibility to seizure. Lee fails to teach or suggest the specific location and extent of disruption of the CRFR2 gene, and further fails to disclose or suggest a phenotype of decreased activity or decreased susceptibility as a result of such a disruption, as recited in these claims. Applicant submits that the issue of the inherency of the phenotypes exhibited by the claimed mouse no longer applies to these claims, as Lee clearly fails to teach or disclose every claimed element.

In view of the disclosure in Lee regarding activity levels noted above, Applicant submits that claims 24-29 are not anticipated by this reference. However, Applicant has submitted new

claims 30-33, which clearly are not anticipated by Lee. Applicant respectfully requests reconsideration and withdrawal of the rejection of claims 24-29 and allowance of claims 24-33.

5. Summary

The claimed mouse does not exhibit any of the phenotypes shown to be exhibited by the mice of the prior art references, including a more robust stress response, increased anxiety behavior, and altered feeding behavior. In fact, the mouse of the instant invention, as presently claimed, exhibits phenotypes distinct from those of the prior art – decreased activity and decreased susceptibility to seizure. None of these phenotypes overlap those observed in the cited references. Furthermore, each of the references cited by the Examiner expressly discloses that their knockout mice do not exhibit activity levels different from wild-type mice, whereas, the claimed mouse has been shown to exhibit **decreased activity** when compared to a wild-type mouse. Therefore, the claimed mouse clearly possesses distinct phenotypes from those of the prior art mice, and more particularly, possesses properties expressly not possessed by the mice described in each of the prior art references. Applicant believes this should be sufficient to overcome each *prima facie* case of anticipation. Applicant has established that the claimed mouse and the mice of the prior art are not identical, and possess distinct and sometimes inconsistent properties. Therefore, Applicant believes that the rejections under 35 U.S.C. § 102 are improper, and respectfully requests withdrawal of the rejections.

It is believed that the claims are in condition for allowance, and notice to that effect is respectfully requested. The Commissioner is hereby authorized to charge any deficiency or credit any overpayment to Deposit Account No. 50-1271 under Order No. R-616.

Respectfully submitted,

Date: _____

9/22/03

Kelly L. Quast

Kelly L. Quast, Reg. No. 52,141

Deltagen, Inc.
1031 Bing Street
San Carlos, CA 94070
Tel. (650) 569-5100
Fax (650) 569-5280